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Case Report

Gonococcal septic shock, acute respiratory distress syndrome, and multisystem organ failure: a case report

Joshua Landy [a], Dennis Djogovic [b], Wendy Sligl [c,*]

[a] Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[b] Department of Emergency Medicine and Division of Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[c] Divisions of Infectious Diseases and Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta, 3C2.12 Walter Mackenzie Health Sciences Centre, 8440-112th St, Edmonton, Alberta, Canada T6G 2B7

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SUMMARY

We describe the first reported case of gonococcal septic shock with associated acute respiratory distress syndrome and multisystem organ failure, in which the patient made a full recovery, and add to the paucity of descriptive literature on gonococcal sepsis. The case was a 36-year-old previously healthy Aboriginal female from northern Canada. Treatment included fluid resuscitation, vasoactive drugs, mechanical ventilation, antimicrobial therapy, corticosteroid replacement, activated protein C, and general supportive care. In addition to being the first reported case of gonococcal septic shock with associated acute respiratory distress syndrome and multisystem organ failure in which the patient made a full clinical recovery this is also the first case of gonococcal septic shock treated with activated protein C; an association between its use and the favorable outcome is postulated, but cannot be confirmed.

Introduction

Gonorrhea is a sexually transmitted infection caused by the bacterium *Neisseria gonorrhoeae*. Gonococcal infection is both preventable and treatable, but despite this remains a cause of significant morbidity including pelvic inflammatory disease, epididymitis, and infertility. Rarely, disseminated infection may result in sepsis or septic shock, with poor prognoses based on previous literature.

Case report

A 36-year-old previously healthy Aboriginal woman with a history of alcohol use was brought to a remote healthcare center in the Canadian North with a several day history of progressive confusion and a 3-week history of lower abdominal pain. On arrival she was hypotensive with a blood pressure of 60/42 mmHg, tachycardic, and oliguric. Glasgow coma score (GCS) was 5, temperature 38.1 °C, respiratory rate 30–35 breaths/min, and oxygen saturation by pulse oximetry was 98% on 4 l by nasal cannulae. She was fluid resuscitated, supported with vasopressors, and intubated. Due to the challenges of arctic winter and distance (over 2000 km) transfer to our tertiary care center required 13 h. Physical examination at the peripheral hospital was non-contributory.

Limited laboratory investigations prior to transfer included: hemoglobin 105 g/l; leukocyte count 11.9×10^9/l (86% neutrophils, no left shift); platelet count 137×10^9/l; creatinine 279 μmol/l (previously documented to be normal); international normalized ratio (INR) 1.7. An arterial blood gas revealed a severe metabolic acidosis with an anion gap of 16. Osmolality and toxic alcohol testing were not available. An ethanol infusion was initiated for possible toxic alcohol ingestion. Empiric ceftriaxone and vancomycin were administered after obtaining blood cultures.

Upon arrival at our intensive care unit (ICU), the patient was comatose and hemodynamically unstable requiring high dose vasopressor support. Urine output improved with fluid resuscitation and an increase in mean arterial pressure – dialysis was not required. The serum osmolal gap was normal; additionally, methanol, ethylene glycol, and isopropanol levels were undetectable. The ethanol infusion was thus discontinued. The patient remained on empiric broad-spectrum antimicrobials and vasopressors for septic shock. Adjunctive corticosteroids were prescribed for vasopressor-dependent septic shock.[1] Admission blood work revealed: leukocyte count 33.4×10^9/l with 24% bands; platelets 111×10^9/l; creatinine 270 μmol/l; lactate 6.1 mmol/l;

* Corresponding author. Tel.: +1 780 407 6755; fax: +1 780 407 1228.
E-mail address: wsligl@ualberta.ca (W. Sligl).

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Figure 1. Multiple left hand purpuric lesions.

troponin 0.85 μg/l; and markedly elevated liver enzymes (alanine aminotransferase (ALT) 5864 U/l, alkaline phosphatase (ALP) 254 U/l, bilirubin 64 μmol/l). Additional laboratory results were not consistent with disseminated intravascular coagulation. Random cortisol was 962 nmol/l. The acute physiology and chronic health evaluation (APACHE) II score calculated within the first 24 h of admission was 30, with a predicted mortality of 70.3%.

Chest radiography demonstrated bilateral patchy alveolar airspace disease with a PaO_2/FiO_2 ratio of 125 and no evidence of left atrial hypertension based on central venous pressure monitoring and 2D-echocardiography. An electrocardiogram demonstrated sinus tachycardia. Initial central venous oxygen saturation was 57%, which improved with inotropic support. An ultrasound of the abdomen demonstrated fatty infiltration of the liver.

On the second day of admission, the peripheral microbiology laboratory reported Gram-negative diplococci from initial blood cultures. The evolving physical examination demonstrated previously undocumented conjunctival suffusion, bilateral knee effusions, and multiple purpuric lesions on the palms, fingers, shins, and soles of the feet (Figure 1). A pustular lesion was noted on the right lateral thigh (Figure 2). Meningismus was not present.

Meningococcemia was suspected and treatment with activated protein C (APC) was initiated after completion of a lumbar puncture 33 h from the time of ICU admission. Cerebrospinal fluid (CSF) parameters were within normal limits, including white blood cell count, protein, glucose, and Gram stain. On the third day of admission however, *Neisseria gonorrhoeae* was confirmed as the blood culture isolate. The isolate was susceptible to ceftriaxone and ciprofloxacin. Given this result, the patient's history of abdominal pain was assumed to be due to pelvic inflammatory disease (PID). A limited gynecological examination was normal.

Figure 2. Pustular lesion noted on the right lateral thigh.

Left knee arthrocentesis did not reveal an inflammatory or septic arthritis. A vaginal specimen was negative for *N. gonorrhoeae* and *Chlamydia trachomatis* by nucleic acid testing (NAT). A vaginal specimen was obtained due to ease of collection and similar sensitivity and specificity for this collection site.[2,3] Pregnancy testing and serology for HIV, syphilis, and hepatitis B were negative. Hepatitis C serology was positive. A transesophageal echocardiogram demonstrated a hyperdynamic left ventricle consistent with distributive shock. Valvular vegetations were not present. Complement levels were globally reduced: C3 0.54 g/l (normal range 0.80–2.00), C4 0.07 g/l (normal range 0.18–0.36), and total hemolytic complement (CH50) <10 kU/l (normal range 22–60). Quantitative immunoglobulins were normal.

The patient gradually improved with mechanical ventilation, vasopressor support, antimicrobials, corticosteroids, APC, and supportive ICU care. Pulmonary, renal, hepatic and cerebral function improved and she was extubated on the twelfth day of hospitalization. She was transferred to the general internal medicine ward two days later and eventually to her home community, with complete recovery of all organ systems. She completed 10 days of intravenous ceftriaxone. On later questioning, the patient denied any symptoms of PID other than lower abdominal pain. A full gynecological examination was to be completed as an outpatient.

Public health was notified and the patient's common-law husband was provided with testing and follow-up.

Discussion

We have no doubt that gonococcal sepsis and septic shock are more common than reflected in the existing literature; epidemiologic descriptions of this condition are sorely lacking.

We could identify only two previously published case reports of gonococcal septic shock, both of which were fatal.[4,5] The first case, described in 1980, involved a 19-year-old male with Hodgkin's disease who underwent splenectomy and radiation therapy. He developed fulminant gonococcemia 12 months later associated with a petechial rash, and died within 18 h of hospital admission. The second case, reported in 2001, was a 53-year-old woman found unconscious in her apartment with a history of heavy alcohol use, liver cirrhosis, and severe malnutrition. The diagnosis and treatment of gonococcemia were delayed, likely contributing to her poor outcome. The patient required mechanical ventilation, and developed multisystem organ failure and refractory shock prior to her death. *N. gonorrhoeae* was isolated from blood cultures in both cases, as in our patient. Reasons for our patient's favorable outcome in comparison to these two fatal cases can only be postulated; immune competence, relatively early diagnosis and treatment, and the use of APC may all have been contributing factors.

Gonococcal sepsis with acute adult respiratory distress syndrome (ARDS) has likewise rarely been reported in the literature. The first two cases, reported in 1976 and 1980, describe immunocompetent patients with gonococcal sepsis who developed hypoxia and acute bilateral pulmonary infiltrates.[6,7] Both patients improved with antimicrobials and one patient received high-dose corticosteroid therapy. Neither of the patients required mechanical ventilation and both made a full recovery. The third reported case in 1991 was the first case to require mechanical ventilation.[8] Measurements of wedge pressure were obtained by pulmonary artery catheterization to rule out cardiac dysfunction. The patient eventually made a full recovery. Our patient, therefore, would be the second reported case of gonococcal sepsis and ARDS requiring mechanical ventilation.

Acquired protein C deficiency may occur in meningococcal infection,[9–11] resulting in a prothrombotic state. Microvascular thrombosis is thought to contribute to multisystem organ failure. APC has profibrinolytic, antithrombotic, and anti-inflammatory properties – resulting in decreased microvascular thrombosis and improved end-organ function. Although somewhat controversial,[12] its use has been shown to decrease morbidity and mortality in patients with septic shock, including those with meningococcemia and particularly those with purpura fulminans.[13–16] *Neisseria meningitidis* and *N. gonorrhoeae* share multiple virulence factors and presumably common pathophysiology in human infection. Lipooligosaccharide endotoxemia causes the release of inflammatory cytokines such as interleukin (IL)-1, IL-6, tumor necrosis factor (TNF), and interferon (IFN)-γ.[17–19] Given this common pathophysiology, APC may also be beneficial in the treatment of gonococcal sepsis, and might have contributed to our patient's favorable outcome.

Deficiencies of both early and terminal components of the complement cascade have been associated with increased susceptibility to neisserial infection.[20–24] Complement deficiency may also result from complement activation in sepsis. We suspect our patient's complement levels were markedly reduced as a result of sepsis and not due to a preexisting deficiency, however follow-up testing will be pursued.

In summary, gonococcal septic shock has rarely been reported, and both previously reported cases resulted in fatal outcomes. This is in contrast to the full recovery observed in the current case despite ARDS and multisystem organ dysfunction. Early diagnosis, young patient age, immune competence, and aggressive sepsis management may have contributed to our patient's favorable outcome.

Conflict of interest: None of the authors disclose any financial or personal relationships with other people or organizations that could inappropriately influence their work. Patient consent for publication was obtained.

References

1. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008;**36**:296–327.
2. Leslie DE, Azzato F, Ryan N, Fyfe J. An assessment of the Roche Amplicor *Chlamydia trachomatis/Neisseria gonorrhoeae* multiplex PCR assay in routine diagnostic use on a variety of specimen types. *Commun Dis Intell* 2003;**27**: 373–9.
3. Masek BJ, Arora N, Quinn N, Aumakhan B, Holden J, Hardick A, et al. Performance of three nucleic acid amplification tests (NAATs) for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using self-collected vaginal swabs recruited from an internet-based screening program. *J Clin Microbiol* 2009; **47**:1663–7.
4. Thiery G, Tankovic J, Brun-Buisson C, Blot F. Gonococcemia associated with fatal septic shock. *Clin Infect Dis* 2001;**32**:E92–3.
5. Austin TW, Sargeant HL, Warwick OH. Fulminant gonococcemia after splenectomy. *Can Med Assoc J* 1980;**123**:195–6.
6. Markham JD, Vilseck Jr JR, O'Donohue Jr WJ. Acute adult respiratory distress syndrome associated with gonococcal septicemia. *Chest* 1976;**70**:667–70.
7. Walters DG, Goldstein RA. Adult respiratory distress syndrome and gonococcemia. *Chest* 1980;**77**:434–6.
8. Belding ME, Carbone J. Gonococcemia associated with adult respiratory distress syndrome. *Rev Infect Dis* 1991;**13**:1105–7.
9. Fourrier F, Lestavel P, Chopin C, Marey A, Goudemand J, Rime A, et al. Meningococcemia and purpura fulminans in adults: acute deficiencies of proteins C and S and early treatment with antithrombin III concentrates. *Intensive Care Med* 1990;**16**:121–4.
10. Powars D, Larsen R, Johnson J, Hulbert T, Sun T, Patch MJ, et al. Epidemic meningococcemia and purpura fulminans with induced protein C deficiency. *Clin Infect Dis* 1993;**17**:254–61.
11. Powars DR, Rogers ZR, Patch MJ, McGehee WG, Francis Jr RB. Purpura fulminans in meningococcemia: association with acquired deficiencies of proteins C and S. *N Engl J Med* 1987;**317**:571–2.
12. Marti-Carvajal A, Salanti G, Cardona AF. Human recombinant activated protein C for severe sepsis. Cochrane Database Syst Rev 2008;(1):CD004388.
13. Bachli EB, Vavricka SR, Walter RB, Leschinger MI, Maggiorini M. Drotrecogin alfa (activated) for the treatment of meningococcal purpura fulminans. *Intensive Care Med* 2003;**29**:337.
14. Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001;**344**:699–709.
15. Ettingshausen CE, Veldmann A, Beeg T, Schneider W, Jager G, Kreuz W. Replacement therapy with protein C concentrate in infants and adolescents with meningococcal sepsis and purpura fulminans. *Semin Thromb Hemost* 1999;**25**:537–41.
16. Vincent JL, Angus DC, Artigas A, Kalil A, Basson BR, Jamal HH, et al. Effects of drotrecogin alfa (activated) on organ dysfunction in the PROWESS trial. *Crit Care Med* 2003;**31**:834–40.
17. Brandtzaeg P, Mollnes TE, Kierulf P. Complement activation and endotoxin levels in systemic meningococcal disease. *J Infect Dis* 1989;**160**:58–65.
18. Girardin E, Grau GE, Dayer JM, Roux-Lombard P, Lambert PH. Tumor necrosis factor and interleukin-1 in the serum of children with severe infectious purpura. *N Engl J Med* 1988;**319**:397–400.
19. Waage A, Brandtzaeg P, Halstensen A, Kierulf P, Espevik T. The complex pattern of cytokines in serum from patients with meningococcal septic shock. Association between interleukin 6, interleukin 1, and fatal outcome. *J Exp Med* 1989;**169**:333–8.
20. Alper CA, Abramson N, Johnston Jr RB, Jandl JH, Rosen FS. Increased susceptibility to infection associated with abnormalities of complement-mediated functions and of the third component of complement (C3). *N Engl J Med* 1970;**282**:350–4.
21. Ellison 3rd RT, Kohler PF, Curd JG, Judson FN, Reller LB. Prevalence of congenital or acquired complement deficiency in patients with sporadic meningococcal disease. *N Engl J Med* 1983;**308**:913–6.
22. Fijen CA, Kuijper EJ, te Bulte MT, Daha MR, Dankert J. Assessment of complement deficiency in patients with meningococcal disease in The Netherlands. *Clin Infect Dis* 1999;**28**:98–105.
23. Petersen BH, Graham JA, Brooks GF. Human deficiency of the eighth component of complement. The requirement of C8 for serum Neisseria gonorrhoeae bactericidal activity. *J Clin Invest* 1976;**57**:283–90.
24. Ross SC, Densen P. Complement deficiency states and infection: epidemiology, pathogenesis and consequences of neisserial and other infections in an immune deficiency. *Medicine (Baltimore)* 1984;**63**:243–73.